REMARKS/ARGUMENTS

Applicants appreciate the Examiner's thoughtful comments in the July 26, 2006 Office Action ("Office Action") and in the December 11, 2006 Advisory Action ("Advisory Action"). With this Amendment, Applicants hope to place the claims in condition for allowance.

Summary of Claim Amendments

Applicants have amended claim 1 in several aspects. First, as suggested by the Examiner, Applicants have amended the preamble of claim 1 to recite "diagnosing bipolar disorder or major depressive disorder in a subject." Also, per the Examiner's suggestion, Applicants have also amended claim 1 to remove the phrase "or is predisposed for." Thus, Applicants claims are now limited to diagnosing a relatively narrow class of mental disorders in patients. Support for these claim amendments is found in the claims as originally filed and in the specification at, *e.g.*, paragraphs 63-65, 66, 89, 165, 202 and 216.

Applicants have also amended claim 1 to address the Examiner's argument for rejecting the claim under 35 U.S.C. § 112, second paragraph. *See* Office Action at page 5. The Examiner stated that "typically, a polynucleotide is not 'encoded' by a nucleic acid per se." *Id.* Applicants have amended claim 1 to more clearly refer to *TBR1 messenger RNA*. Support for this amendment may be found in the specification at, *e.g.*, paragraphs 18 and 208. To avoid a lack of antecedent basis, the phrase "sample" has also been replaced by the phrase "TBR1 messenger RNA" in step (iii) of claim 1. Applicants have also amended the claim to refer to the use of a complementary nucleic acid probe for detecting TBR1 messenger RNA transcripts. Support for this amendment may be found in the claims as originally filed and in the specification at, *e.g.*, paragraphs 90-98 and 208-210.

Applicants have also amended claim 1 to limit the claim to the detection of RNA expression in isolated *dorsolateral prefrontal cortex* tissue. Support for this amendment may be found in the specification at, *e.g.*, Example 1, paragraph 204.

Applicants have also amended claim 52 to change the dependency to claim 1 instead of canceled claim 8. Applicants have also added claim 53 which is limited to the diagnosis of

major depressive disorder. Both of these claims (*i.e.*, amended claim 52 and new claim 53) are limited to the diagnosis of each of the specific mental disorders recited in claim 1 and, by virtue of their dependency on claim 1, incorporate all of the limitations of claim 1. Thus, no new matter is added.

During a phone call with the Examiner following the submission of Applicants' substitute Amendment After Final, the Examiner indicated that if an RCE was filed, the Examiner would search the second mRNA marker recited in the original claim set, *i.e.*, the CAMKII-α gene.[2] In that regard, Applicants have added new claims 54-55 which are drawn to diagnosing bipolar disorder by detecting increased CAMKII-α gene expression in a subject's isolated dorsolateral prefrontal cortex. Support for this claim may be found in the claims as originally filed and in the specification at, *e.g.*, paragraphs 204, 214, and 216.

Finally, Applicants have canceled claim 3 (the limitation in claim 3 relating to a "nucleic acid" reagent is now incorporated in claim 1) and claims 8-11, without prejudice.

Remark regarding Advisory Action

Applicants' amended claims are a sincere attempt to narrow the scope of the pending claims using language intended to satisfy the Examiner's concerns with respect to definiteness and enablement. Applicants' respectfully submit that the amendments presented here render moot each of the Examiner's rejections in the July 26, 2006 Office Action.

The December 11, 2006, "Advisory Action" states the following:

> [T]he amendment is not entered because it brings up issues of both new matter and 35 U.S.C. § 112, 2nd paragraph, for being indefinite. In particular, in claim 1, step (ii), says "a messenger RNA encoded by a gene with at least 95% identity." It is not known what 95% refers to, the mRNA or the gene. Further, applicant has claimed a "reagent" that binds variants 95% identical to SEQ ID No: 3, however the examiner cannot find support for a reagent that selectively binds variants of 95%. In addition, the

[2] Detection of CAMKII-α (i.e., SEQ ID No. 1) gene expression was one of the *species* identified by the Examiner on page 6 of the August 30, 2005 Restriction Requirement relating to this application.

> specification and the art do not support a generic "reagent that selectively associates with a messenger mRNA of SEQ ID NO: 3."

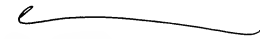
Applicants' presently amended claims do not raise the issues described in the Advisory Action. Rather, Applicants' claims describe in definite terms a method for diagnosing a limited set of mental disorders by measuring the levels of *specific* messenger RNA molecules (*i.e.*, TBR1 or CAMKII-α) using nucleic acid probes. Applicants respectfully submit that, as of the priority date of their application, the design of complementary nucleic acid probes for specifically detecting and measuring the expression of a known gene was well-known in the art. To the extent that any experimentation would be required to identify a suitable probe, such experimentation is minimal and routine. The specification outlines the standard, well-known procedures for identifying suitable nucleic acid probes for use in the claimed methods (see, *e.g.*, paragraphs 46-47 and 89-104) and also provides instructions and materials tailored expressly for this purpose (see, *e.g.*, paragraphs 71 and 75. In addition, the specification provides examples of suitable probes which were successfully and easily identified using these very methods. See, *e.g.*, Figures 1 and 3 and paragraph 208 (describing the transcription of TBR1 and CAMKII-α riboprobes).

Applicants respectfully remind the Examiner that they are not asserting here to have discovered a novel or non-obvious nucleic acid *composition*. Rather, Applicants' pending claims recite *methods* of diagnosing a limited and specified set of mental disorders by assaying the tissue-specific expression of recited messenger RNA molecules using appropriate nucleic acid probes. For the reasons provided above, Applicants respectfully submit that they have taught *one of skill in the art* how to diagnose the recited mental illnesses using any complementary nucleic acid probes which bind specifically to TBR1 or CAMKII-α messenger RNA.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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